THE CLAIMS

1. (original) A polypeptide comprising a single-domain of the variable region of the heavy chain of an antibody molecule, which is soluble and stable and capable of binding a specific antigen of interest, said polypeptide comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising at least one charged residue.

2. (original) The polypeptide of claim 1 wherein the polypeptide is substantially monomeric.

3. (original) The polypeptide of claim 1, wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, having a unique VH/VL interface comprising at least one charged residue and a randomized CDR3.

4. (original) The polypeptide of claim 3 wherein the selected clone is produced in E. coli as insoluble inclusion bodies and the isolated polypeptide is subsequently refolded in-vitro and purified.

5. (original) The polypeptide claim 3 wherein the scaffold element representing the VH/VL interface comprises the sequence Lysine-44, Leucine-45, and Tryptophan-47.

6. (original) The polypeptide of claim 1 wherein the specific antigen of interest is an immunoglobulin molecule.

7. (original) The polypeptide of claim 3 wherein the CDR3 sequence between residues 95 and 100 C comprises the consensus sequence: Gly-X-Ser-Pro-Gln, wherein X represents any amino acid.

8. (original) The polypeptide of claim 3 wherein the CDR3 sequence between residues 95 and 100 C is selected from the sequences: Gln-Ser-Gly-Gln-Ser-Pro-Gln-- Ser-Ile, and Asn-Gly-Lys-Ser-Pro-Gln-Ala-Ala-Trp.

9. (original) The polypeptide of claim 1 wherein the specific antigen of interest is tumor necrosis factor.

10. (original) The polypeptide of claim 9 wherein the CDR3 sequence between residues 95 and 100 C comprises the sequence: Phe-Pro-Thr-Gly-Asp-Leu-Ala-Glu-Lys.

11. (original) The polypeptide of claim 1 wherein the specific antigen of interest is Streptavidin.

12. (original) The polypeptide of claim 11 wherein the CDR3 sequence between residues 95 and 100 C is selected from the sequences: His-Ala-Gln-Arg-Arg-Pro-Trp-- Ile-Arg, and Glu-Asp-Pro-His-Pro-Gln-Arg-Gly-Tyr.

13. (original) A peptide capable of binding a specific antigen of interest, said peptide being derived from the randomized sequence of the CDR3 region of a polypeptide comprising a single-domain of the variable region of the heavy chain of an antibody molecule, which is soluble and stable and capable of binding said specific antigen of interest, said polypeptide comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising at least one charged residue.

14. (original) The peptide of claim 13 wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, having a unique VH/VL interface comprising at least one charged residue and a randomized CDR3.

15. (original) The peptide of claim 13 wherein the peptide comprises 4-20 amino acids.

16. (original) The peptide of claim 13 wherein the peptide comprises 7-15 amino acids.

17. (original) The peptide of claim 13 wherein the specific antigen of interest is an immunoglobulin molecule.

18. (original) The peptide of claim 13 wherein the specific antigen of interest is tumor necrosis factor.

19. (original) A pharmaceutical composition comprising as an active ingredient the polypeptide of claim 1, and a physiologically acceptable diluent or carrier.

20. (original) A pharmaceutical composition comprising as an active ingredient the peptide of claim 13, and a physiologically acceptable diluent or carrier.

21-33. cancelled.

34. (new) The pharmaceutical composition of claim 19 wherein the polypeptide is substantially monomeric.

B1

35. (new) The pharmaceutical composition of claim 19 wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, having a unique VH/VL interface comprising at least one charged residue and a randomized CDR3.

36. (new) The pharmaceutical composition of claim 35 wherein the selected clone is produced in E. coli as insoluble inclusion bodies and the isolated polypeptide is subsequently refolded in-vitro and purified.

37. (new) The pharmaceutical composition of claim 35 wherein the scaffold element representing the VH/VL interface comprises the sequence Lysine-44, Leucine-45, and Tryptophan-47.

38. (new) The pharmaceutical composition of claim 35 wherein the CDR3 sequence between residues 95 and 100 C comprises the consensus sequence: Gly-X-Ser-Pro-Gln, wherein X represents any amino acid.

39. (new) The pharmaceutical composition of claim 35 wherein the CDR3 sequence between residues 95 and 100 C is selected from the sequences: Gln-Ser-Gly-Gln-Ser-Pro-Gln-- Ser-Ile, and Asn-Gly-Lys-Ser-Pro-Gln-Ala-Ala-Trp.

40. (new) The pharmaceutical composition of claim 19 wherein the CDR3 sequence between residues 95 and 100 C comprises the sequence: Phe-Pro-Thr-Gly-Asp-Leu-Ala-Glu-Lys.

41. (new) The pharmaceutical composition of claim 19 wherein the specific antigen of interest is Streptavidin.

42. (new) The pharmaceutical composition of claim 20 wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, having a unique VH/VL interface comprising at least one charged residue and a randomized CDR3.

43. (new) The pharmaceutical composition of claim 20 wherein the peptide comprises 4-20 amino acids.

44. (new) The pharmaceutical composition of claim 20 wherein the peptide comprises 7-15 amino acids.